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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,118	02/12/2002	Jerome Becquart	6832.1429-03000	2328

7590 10/22/2003

FINNEGAN, HENDERSON, FARABOW, GARRETT AND DUNNER
1775 K Street, N.W.
Washington, DC 20006

EXAMINER	
GUZO, DAVID	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	10/073,118	BECQUART ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 8/13/03.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 and 2 is/are rejected.

7)☒ Claim(s) 3-29 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 12 February 2002 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on 07 June 2002 is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 07/561,879 .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The Drawing Changes submitted 06/07/02 are approved by the examiner. Revised Drawings must be submitted in response to this Office Action. Deferral of submission of revised drawings is no longer permitted (See 37 CFR 1.85).

1. Claims 3-29 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and/or cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 3-29 have not been further treated on the merits.

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-2 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,165,470 (hereafter the '470 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. The subject matter of claim 1 in the '470 patent is entirely encompassed within the scope of the instant claims, in other words, claim 1 of the '470 patent anticipates the instant claims. Specifically, the instant claims recite any hybrid macromolecule comprising the active domain of a receptor (a membrane receptor) for a given virus or the active domain of a molecule which can bind a given virus coupled to albumin or a variant of albumin while the '470 patent recites a species of the instant claims wherein the species is a hybrid peptide comprising the active domain of the CD4 receptor (a membrane receptor) of HIV wherein the N-terminus of said domain is covalently coupled to albumin or a derivative of albumin.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' claims read on a genus of hybrid macromolecules comprising albumin or a variant of albumin coupled to the active domain of any receptor for any virus or any active domain of a molecule which can bind to any virus or the active domain of any receptor of any ligand intervening in any pathological process. With the exception of the CD4 receptor of HIV coupled to albumin, applicants have not provided an adequate written description of the claimed invention.

The written description requirement for a claimed genus can be satisfied through sufficient description of a representative number of species by actual reduction to practice, by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the present case, applicants reduce to practice no examples of any hybrid molecules (other than the disclosed CD4-albumin molecules) with the claimed function. Applicants present no examples of the active domains of receptors for any given virus, no examples of active domains of molecules that bind viruses, no examples

of the active domains of receptors of ligands intervening in pathological processes, etc. Applicants do not identify any relevant characteristics of the disclosed CD4 molecules that would provide the skilled artisan with knowledge of the structures of other active domains of receptors for other viruses or pathological processes. Applicants claim the hybrid molecules by function only without any disclosed or known correlation between the structure of the receptor active domains that bind other viruses or mediate pathological processes and the function of said receptor active domains. Therefore, the skilled artisan would not conclude that applicants were in possession of the claimed genus.

6. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for hybrid peptides comprising the V_1 domain or V_1V_2 domains of the CD4 receptor of HIV coupled to albumin or a variant of albumin, does not reasonably provide enablement for any hybrid macromolecule comprising any active domain of any receptor for any virus, any active domain of a molecule which can bind a virus, any active domain of a receptor of a ligand intervening in a pathological process coupled with albumin or a variant of albumin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d

1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Unpredictability of the art. The art in the area of determining and isolating the active domains of receptors of viruses or receptors of ligands that intervene in pathological processes is unpredictable. The research required to determine active domains of receptors involves complex molecular modeling of the receptor molecule in its' natural conformation(s) on the surface of a cell. It is difficult or impossible to *a priori* predict the active domain(s) of a receptor molecule from a purified preparation of the protein or even from the amino acid sequence of the receptor. It is difficult or impossible to predict whether the active domain of a receptor would retain its' function as a receptor if it is removed from the rest of the receptor molecule or if it is removed or isolated from its' natural milieu on the cell surface or if it is coupled with a heterologous protein such as albumin.

2) State of the art. The art with regard to generating hybrid molecules comprising active domains or receptors of viruses or active domains of ligands intervening in pathological processes coupled to heterologous molecules such as albumin wherein the receptors maintain their ability to bind the virus or intervene in a pathological process and hence serve as decoys is poorly developed or nil.

3) Number of working examples. With the exception of CD4-albumin molecules, applicants present no working examples of the claimed invention.

4) Amount of guidance provided by applicants. Applicants present no guidance on the practicing of the claimed invention with any other molecules other than CD4 and albumin. Applicants present no teachings on any other active domains of any other virus receptor molecules, no teachings on active domains of any receptor of any ligand intervening in a pathological process, no teachings on the generation of any hybrid molecules comprising said active domains of receptors coupled with albumin, etc.

5) Scope of the claims. The claimed invention is extremely broad in scope. The invention reads on any hybrid macromolecule comprising any active domain of any receptor for any virus or any active domain of any molecule that binds any virus or any active domain of any receptor of a ligand intervening in any pathological process.

6) Nature of the invention. The invention involves complex, unpredictable, aspects of protein structure, protein-protein interactions, design of novel hybrid molecules with unpredictable properties and unpredictable aspects of designing novel therapeutic agents for treatment or prevention of viral infection or disease.

7) Level of skill in the art. The level of skill in the art is high; however, given the complex, unpredictable aspects of the invention, the lack of guidance presented by applicants, the lack of working examples and the broad scope of the invention, it must be considered that the skilled artisan would have had to have conducted undue and excessive experimentation in order to practice the claimed invention.

Given the analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to have practiced essentially trial and error

experimentation in order to try to practice the claimed invention. Said experimentation must be considered to be undue and excessive.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2 are rejected under 35 U.S.C. 102(e) as being anticipated by Hammonds et al.

Applicants claim a hybrid macromolecule that carries the active domain of a receptor (which can be a membrane receptor) of a ligand intervening in a pathological process coupled with albumin.

Hammonds et al. (U.S. Patent 4,857,637, issued 8/15/89, filed 6/12/87, see whole document, particularly column 4, lines 26-38; the paragraph bridging columns 4-5; column 8 and claims 1-10) recites hybrid macromolecules which can comprise a membrane receptor polypeptide sequence (preferably containing the active ligand binding site, see column 12, and which can be a membrane receptor such as EGF receptor) covalently linked to a peptide such as bovine serum albumin. Hammonds et al. notes that cell surface receptors such as EGF have ligands which can be involved in pathological processes such as tumorigenesis.

It is noted that this Office Action contains rejections of the same claims under 35 USC 112, 1st (scope of enablement) and 35 USC 102(e). While these rejections may seem contradictory, they are not because each is based upon a different legal analysis, i.e. sufficiency of the disclosure of the instant application to support claims under 35 USC 112, 1st paragraph vs. sufficiency of a prior art disclosure to anticipate or render obvious an embodiment(s) of the claimed invention (See *In re Hafner*, 161 USPQ 783 (CCPA 1969)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and dependent claim 2) are vague in the use of the word "carries" with regard to the phrase "...either the active domain..." of the receptor or ligand coupled to albumin or a variant of albumin because it is unclear if the hybrid macromolecule is composed of the recited components or instead "carries" these components in addition to some additional (unspecified) components. Claim 1 is also vague in the phrase "...ligand intervening in a pathological process..." because it is unclear what "intervening" in a pathological process encompasses. Claims 1 and 2 are vague in the recitation of the term "active domain of a receptor", it is unclear if this refers exclusively to the ligand binding site on the receptor or to some other aspect of the receptor.

Also, in Claim 1, the phrase "characterized by the fact" is clumsy and does not impart any patentable weight to the claim. When claiming a composition of matter, applicants are encouraged to use legally defined transitional phrases such as "comprising" or "consisting of". For example, in the instant case, redrafting the claim to recite "A hybrid macromolecule comprising (or consisting of) the active domain..." would be remedial.

With regard to the format of the claims, the following is noted:
While there is no set statutory form for claims, the present Office practice is to insist that each claim must be the object of a sentence starting with "I (or we) claim," "The invention claimed is" (or the equivalent). If, at the time of allowance, the quoted terminology is not present, it is inserted by the Technology Center (TC) technical support staff. Therefore, the claims should begin with an article such as "A" or "The" (See MPEP 608.01(m)).

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (703) 305-1998. The fax phone

number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
October 15, 2003

DAVID GUZO
PRIMARY EXAMINER